Official Title:	**A Randomized, Parallel-Group Study to Evaluate the Efficacy and Tolerability of two Dosing Regimens of CTP-543 in Adult Patients With Moderate to Severe Alopecia Areata**
NCT Number:	NCT03941548
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16.1.9 Documentation of Statistical Methods

CP543.2003 Statistical Analysis Plan V1.0, 08 January 2020

[redacted]

Statistical Analysis Plan

Study Title:	**A RANDOMIZED, PARALLEL-GROUP STUDY TO EVALUATE THE EFFICACY AND TOLERABILITY OF TWO DOSING REGIMENS OF CTP-543 IN ADULT PATIENTS WITH MODERATE TO SEVERE ALOPECIA AREATA**
Protocol Number and Version:	**CP543.2003; Amendment 2 dated 25 July 2019**
Product:	**CTP-543**
Sponsor:	**Concert Pharmaceuticals, Inc.** **65 Hayden Avenue, Suite 3000N,** **Lexington, MA** **USA, 02421**
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Prepared by:	[redacted]

[redacted]	**STATISTICAL ANALYSIS PLAN, Final v1.0**
Protocol Number CP543.2003	Sponsor: Concert Pharmaceuticals, Inc.

STATISTICAL ANALYSIS PLAN REVISION SUMMARY			
Version	**Version Date**	**Author**	**Summary of Changes**
Final v1.0	08-Jan-2020	[redacted]	Initial version

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TABLE OF CONTENT

ABBREVIATIONS

Abbreviation or Specialist Term	Explanation
AE	Adverse event
ATC	Anatomic therapeutic chemical
BID	Twice daily
BRS	Back quadrant raw score
CGI-I	Clinical Global Impression of Improvement
CGI-S	Clinical Global Impression of Severity
CI	Confidence interval
CMH	Cochran-Mantel-Haenszel
CRO	Clinical research organization
CS	Clinically significant
CTCAE	Common terminology criteria for adverse events
ECG	Electrocardiogram
ET	Early termination
HBV	Hepatitis B virus
HCV	Hepatitis C virus
LOCF	Last Observation Carried Forward
LRS	Left quadrant raw score
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent-to-treat
NCS	Not clinically significant
PCS	Potentially clinically significant
PGI-I	Patient Global Impression of Improvement
PGI-S	Patient Global Impression of Severity
PP	Per protocol
PPD	Purified protein derivative
PT	Preferred term
QD	Once daily

Abbreviation or Specialist Term	Explanation
QTc	QT interval corrected for heart rate
QTcF	QT interval corrected for heart rate (Fridericia's method)
RRS	Right quadrant raw score
SALT	Severity of Alopecia Tool
SAP	Statistical analysis plan
SD	Standard deviation
SEM	Standard error of the mean
SOC	System organ class
TEAE	Treatment-emergent adverse events
TLF	Table, Listing, and Figure
TRS	Top quadrant raw score
VAS	Visual Analog Scale
WHO-DD	World Health Organization Drug Dictionary
WOCF	Worst observation carried forward

1 INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned analyses and reporting for Concert Pharmaceuticals, Inc. clinical protocol CP543.2003. The analyses described in the SAP are based on protocol amendment 2 dated 25-Jul-2019 and any changes from the protocol-specified analyses will be documented in the SAP prior to database lock. If additional analyses are required to supplement the planned analyses described in this SAP after the database lock, they may be completed and will be described in the CSR.

This SAP has been developed prior to database lock, study unblinding, and final analyses. All final analyses will be performed after the approval of the SAP, clinical trial data are entered into the database, any discrepancies in the data are resolved, determination of the inclusion/exclusion of each subject from each analysis population, lock of the database, and study unblinding.

2 STUDY OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS
Primary	
To compare the efficacy and tolerability of a 24 mg total daily dose of CTP-543 utilizing two different dosing regimens in adult patients with chronic, moderate to severe alopecia areata.	Primary efficacy endpoint in each dose regimen:
	• Relative change in Severity of Alopecia Tool (SALT) score for each dose regimen from Baseline at Week 24.
	Tolerability endpoints in each dose regimen:
	• Adverse events (AEs), vital signs, concomitant medications, clinical laboratories, and electrocardiogram (ECG) results, as well as physical examinations
Secondary/Exploratory	
To assess the proportion of patients achieving defined threshold reductions in SALT score, and for patients to assess their eyebrows, hair coverage and hair coverage quality.	Secondary efficacy endpoints in each dose regimen:
	• Proportion of patients achieving at least a 90%, 75%, and 50% reduction in SALT score from Baseline at Weeks: ○ 4, 8, 12, 16, 20, and 24 in the Treatment Period • Absolute change in SALT scores from Baseline at Weeks: ○ 4, 8, 12, 16, 20, and 24 in the Treatment Period

OBJECTIVES	ENDPOINTS
	• Relative change in SALT scores from Baseline at Weeks: ○ 4, 8, 12, 16, and 20 in the Treatment Period • Change in satisfaction of hair coverage as reported by the patient from Baseline to Weeks 8, 12, and 24
	Exploratory efficacy endpoints in each dose regimen:
	• Change in patient's eyebrows as measured by the patient's Visual Analog Scale (VAS) from Baseline to Weeks 12 and 24 • Change in satisfaction of hair coverage quality as reported by patient from Baseline to Weeks 8, 12, and 24

3 STUDY DESIGN

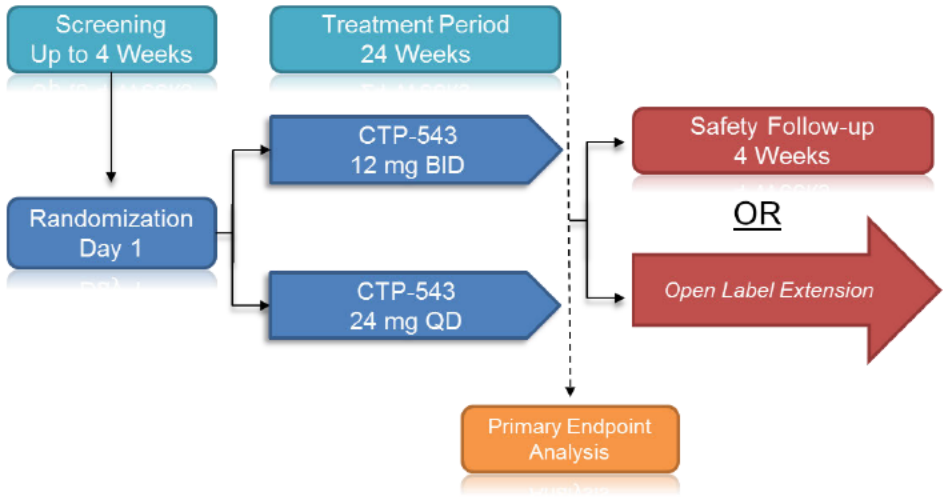
3.1 Overall Design

This is a randomized, parallel-group, multicenter study to evaluate the efficacy and tolerability of two dosing regimens of CTP-543 (12 mg twice daily [BID] vs 24 mg once daily [QD]) in adult patients with chronic, moderate to severe alopecia areata. Patients will be between 18 and 65 years of age and experiencing an episode of alopecia areata lasting at least 6 months and not exceeding 10 years, with at least 50% hair loss as measured by the Severity of Alopecia Tool (SALT) at Screening and Baseline, and are not concurrently being treated for alopecia areata with other treatments that might affect hair regrowth or immune response. Up to approximately 75% of alopecia areata patients with alopecia totalis or universalis, and no more than 10% of patients with alopecia ophiasis will be enrolled.

A full list of the inclusion and exclusion criteria can be found in Sections 7.1 and 7.2 in the CP543.2003 Protocol.

Patients may be screened up to 28 days prior to initiation of study drug. The Treatment Period is a 24-week dosing period where patients will be randomized to receive either 12 mg BID or 24 mg QD of CTP-543.

Figure 1: Study Design



Patients will provide informed consent prior to completing any screening procedures. Patients meeting screening criteria will continue to the Day 1 Randomization Visit for review of eligibility and Baseline assessments. Patients meeting all eligibility criteria will be randomized to receive either 12 mg BID CTP-543 or 24 mg QD CTP-543 in a 1:1 ratio. Approximately 60 patients are planned to be randomized in the study (i.e., approximately 30 patients per dosing regimen).

Patients will take the first dose of study drug in the clinic on Day 1 and will be instructed to take study drug every 12 hours. To minimize the bias in the evaluation of study endpoints, patients, investigators, and site personnel will be unaware of the active drug dosing regimen by administering 2 x 12 mg tablets and 2 x placebo tablets 12 hours apart from each other for the 24 mg QD study drug. Patients should dose study drug in the clinic on all Study Visit Days after clinical laboratory blood draws are completed.

Patient safety will be monitored throughout the trial. Significant cytopenias or other hematologic abnormalities will be managed by severity through dose interruption, or discontinuation, and signs and symptoms of infection will be closely monitored and treated promptly. Patients who experience intolerable symptoms during treatment may discontinue the study at the discretion of the Investigator. Patients may withdraw consent at any time. A patient who prematurely discontinues study drug should have all Week 24 assessments performed as an Early Termination (ET) visit and return for the Safety Follow-up Visit. The Safety Follow-Up Visit may be waived by the Sponsor in instances where patients have discontinued dosing prior to the ET visit on a case-by-case basis.

Upon completion of the 24-week Treatment Period, patients will be eligible to either complete treatment and exit the study following the safety follow-up visit, or roll-over into an open-label extension study.

Appendix 1 provides a description of the procedures planned at each visit.

3.2 Treatment Regimens

CTP-543 will be dosed orally as tablets. Doses and frequency will be allocated as follows:

- 12 mg BID CTP-543 (1 x 12 mg and 1 x placebo tablet every 12 hours)
- 24 mg QD CTP-543 (2 x 12 mg in the mornings and 2 x placebo tablets in the evenings)

3.3 Randomization, Replacement, and Unblinding Procedures

Patients meeting all inclusion criteria and none of the exclusion criteria will be randomized to 12 mg BID CTP-543 or 24 mg QD CTP-543 in a 1:1 ratio. Randomization will be stratified by classification of alopecia areata subtype into one of the following three categories: 1) alopecia areata, 2) alopecia totalis or alopecia universalis, or 3) alopecia ophiasis.

Patients who withdraw or are withdrawn from the study will not be replaced.

To maintain the blind for investigators, subjects, and site personnel, subjects will take their randomized treatment in the am and pm no matter which regimen they are randomized to. The Clinical Research Organization (CRO) study team will also remain blinded to the dosing regimen until database lock.

The study will be unblinded after approval of the SAP, clinical trial data are entered into the database, any discrepancies in the data are resolved, determination of the inclusion/exclusion of each subject from each analysis population and lock of the database.

3.4 Changes to the Analysis from the Protocol

The Efficacy analysis population described in the synopsis of the protocol is referred to as the modified Intent-to-Treat (mITT) analysis population in Section 11.3 of the protocol. To avoid confusion, this analysis population will be called the mITT analysis population in this SAP as well as in the statistical outputs.

As per Section 11.4.3 of the protocol, the total number of days on study drug will exclude dose interruptions. However, dose interruptions will not be excluded from the duration of exposure to the study drug as specified in Section 11, in order to be in line with industry's standards.

As per Section 11.4.4 of the protocol, treatment-emergent AEs (TEAEs) are defined as any AE that occurs after administration of the first dose of study drug until Week 24 or Early Termination Visit. However, TEAEs will be defined as any AEs with onset date/time on or after the first dose of study drug (refer to Section 13.1), in order to be in line with the industry's standards.

As per Section 11.4.4 of the protocol, the number and percentage of patients with abnormal, clinically significant laboratory values (per Investigator judgment) will be summarized by dosing regimen for each clinical laboratory variable. This summary has been replaced by shift tables from Baseline to the worst post-Baseline result describing shifts to abnormality as assessed by the central laboratory (low, normal, high) (refer to Section 13.2). Abnormal, clinically significant laboratory values (per Investigator judgement) will be identified in by-patient data listing.

4 POPULATIONS FOR ANALYSIS

4.1 Modified Intent-to-Treat Analysis Population

The mITT analysis population will include all randomized patients who receive at least one dose of study drug and have at least 1 post-treatment SALT assessment. Patients will be summarized according to study drug regimen to which they were randomized. This analysis population will be the main analysis population for the efficacy analyses.

4.2 Per Protocol Analysis Population

The Per Protocol (PP) analysis population will include all mITT subjects with no major protocol deviation (i.e., a major protocol deviation is defined as a protocol deviation that may alter or confound interpretation of the study results). The classification of each protocol deviation as major or not will be done prior to the database lock. Analyses based on this analysis population will be performed only if 10% or more of mITT patients have at least one major protocol deviation. Patients will be summarized according to study drug regimen to which they were randomized. This analysis population will be used to perform supportive efficacy analyses.

4.3 Safety Analysis Population

The Safety analysis population will include all patients who received at least one dose of study drug. Patients will be summarized according to study drug regimen received (i.e., as treated) should it differ from the randomized study drug regimen.

5 GENERAL CONSIDERATIONS

Formats and layouts of tables, listings, and figures (TLFs) will be provided in a separate document (output general layout is described in Appendix 2). Minor changes to the mocks after formal SAP approval will not necessitate re-approval unless changes to the text of the SAP are required.

5.1 Baseline

Unless otherwise specified, Baseline value will be defined as the last non-missing assessment prior to the first dose of study drug (including repeat and unscheduled assessments). If the last non-missing assessment is performed on the same date as the first dose of study drug and time is not available, the assessment will be considered as Baseline, except for adverse events (AEs) and medications starting on the first study treatment dose date which will be considered post-Baseline.

5.2 Reference Start Date and Study Day

Study days will be calculated from the date of the first dose of study drug regimen and will be used to show start/end day of assessments or events.

Study day = (Date of event – Date of first dose) + 1 if date of event is on or after the date of first dose of study regimen;

= (Date of event – Date of first dose) if date of event is before the date of first dose of study regimen;

In situations where the assessment/event start/end date is partially or completely missing, study start/end day will be missing.

5.3 Windowing Conventions

For scheduled visits, there will be no reassignment of the analysis visit based on date, and all data will appear in summary tables based on the nominal timepoint.

Both unscheduled visits and repeat visits will be reassigned to the closest prior visit. If an assessment was already documented at that visit, the scheduled data will be used in summaries. If the scheduled data was missing, then the re-assigned unscheduled visit/repeat visit will be used in summaries.

5.4 Handling of Repeats, Unscheduled Visits, and Early Termination Data

See Section 5.3 for handling of unscheduled and repeat visits.

Early termination visit assessments will be summarized as a separate visit.

All data from repeat, unscheduled visits, and early termination visits will be listed.

6 STATISTICAL CONSIDERATIONS

6.1 Sample Size

A sample size of 25 patients (completers) per group provides adequate precision for the estimated dosing regimen difference for relative change in SALT score from Baseline at Week 24. Precision of the estimated difference is quantified by the width of the 90% confidence intervals (CI) for the dosing regimen difference.

6.2 Descriptive Statistics and Common Derivations

Continuous endpoints will be summarized using descriptive statistics (i.e., number of subjects with non-missing data, mean, standard deviation [SD], median, minimum and maximum). Categorical endpoints will be presented as frequencies and percentages. Unless otherwise indicated, the percentages will be computed based on the number of patients included in the concerned analysis population.

Summary tables will be presented by dosing regimen and visit, when applicable.

As the SALT score is by nature a measurement of total surface of the scalp without hair, it is important to note that in the context of this SAP, SALT endpoints will follow these definitions:

> Absolute change from Baseline = difference in SALT measurements i.e., Baseline SALT score - post-Baseline SALT score
>
> Relative change from Baseline = percent change of the post-Baseline SALT score, where baseline SALT score is the denominator i.e. (absolute change from Baseline / Baseline SALT score) * 100%

For all other endpoints (e.g., patient satisfaction hair coverage, VAS, patient satisfaction hair coverage quality, clinical laboratory, vital signs, etc.), the change and percent change from baseline will be computed as follows:

> Change from Baseline = Assessment value at post-Baseline visit X – Baseline value.
>
> Percent change from Baseline = (change from Baseline / Baseline value]) * 100%.

6.3 Handling of Dropouts or Missing data

See Appendix 3 for handling of completely or partially missing dates for prior and concomitant medications and AEs. Imputed AE onset and end dates/medication start and stop dates will only be used for the determination of the treatment-emergent/concomitant status. That is, they will not be used to compute any study day or duration and will not be presented in the by-patient data listings.

For the SALT endpoints (e.g., absolute and percent changes from baseline as well as achieving at least 50%, 75%, 80%, and 90% reduction and having a SALT score $\leq$ 10 and $\leq$ 20, the Last Observation Carried Forward (LOCF) approach will be implemented for missing SALT score data, e.g., if the SALT score in the Week 16 visit window is missing, the next and closest available on-treatment SALT score measurement before the Week 16 visit window will be used for all remaining SALT assessments: Week 16, Week 20 and Week 24. Missing baseline values will not be carried forward. If a SALT assessment is missing between two non-missing SALT assessments visits, the SALT score at that visit will be interpolated using the mean of the closest pre- and post-assessments.

All other missing efficacy data as well as missing safety data will not be imputed.

6.4 Statistical Tests

No formal hypothesis tests will be conducted. Only two-sided confidence intervals (CIs) at the 90% coverage will be presented. Nominal p-values will be provided.

6.5 Multiple Comparisons/Multiplicity

No adjustment for multiple comparisons and multiplicity will be done for this study since no formal inferential testing will be performed.

6.6 Interim Analysis

No interim analysis is planned for this study.

6.7 Multicenter Studies

Patients will be enrolled at approximately 12 sites. To reduce variability, one rater should perform each clinician dependent assessments for an individual patient for the duration of the study. All investigators using the SALT will be trained prior to use. Data from all sites will be pooled in the summaries and figures

6.8 Adjustments for Covariates

Not applicable.

6.9 Examination of Subgroups

The analysis of the primary and secondary efficacy endpoints will be repeated for the following subgroups (refer to Section 8 for the definition of each alopecia areata subtype):

- Subjects with alopecia areata at Baseline;
- Subjects with alopecia totalis or alopecia universalis at Baseline;
- Subjects with alopecia ophiasis at Baseline

6.10 Software Version

All analyses will be performed using SAS® software version 9.4 or higher.

7 STUDY SUBJECTS

7.1 Disposition of Subjects

Disposition will be summarized by randomized dosing regimen for all patients who provide informed consent. The following disposition information will be summarized (percentages based on the number of subjects randomized within each dosing regimen, with the exception of the screen failure and reasons for discontinuation):

- The number of patients screened;
- The number and percentage of screen failures. For the percentage of screen failures, the denominator will be the number of patients screened.
- The number of patients randomized;
- The number and percentage of patients within the Safety, mITT and PP analysis populations (if applicable);
- The number and percentage of patients who completed the study, defined as:
    - Completing Visit 10 (Week 24) and Visit 11 (Week 28)
    - Completing Visit 10 (Week 24) and enrolling into the open-label extension

  - Completing Visit 10 (Week 24) but did not roll into the open-label extension and did not complete the safety follow up visit.

- The number and percentage of patients who prematurely discontinued, and the frequency and percentage of each discontinuation reason. The denominator for the percentage of each discontinuation reason will be the number of patients who discontinued.

A listing of patient's disposition and a listing of patient's randomization information will be provided. A listing of patients included and excluded from each of the analysis population will also be provided. Patient data listings will list date of informed consent, date of first/last treatment, date of end of study/early termination, and reasons for discontinuation.

7.2 Protocol Deviations

An important protocol deviation is defined as a protocol deviation that might significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a subject's rights, safety, and/or well-being. The frequency and percentage of patients with at least one important protocol deviation will be summarized by deviation category and dosing regimen based on the Safety analysis population. Non-important and important protocol deviations will be summarized by randomized dosing regimen, classification, and category for all randomized patients and listed by patient in a data listing.

A data review will be conducted before database lock by the Medical Monitor and the sponsor to classify protocol deviations as minor or major. Deviations that may alter or confound interpretation of the study efficacy results will be classified as major deviations. Minor and major protocol deviations will be summarized by randomized dosing regimen, classification, and category for all randomized patients and listed by patient in a data listing.

8 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographics and Baseline characteristics will be collected at the screening visit, between Day - 28 and -1, and will be summarized by dosing regimen with descriptive statistics based on the Safety analysis population. The list of demographics and Baseline characteristics to be summarized include:

- Age (years) – calculated relative to date of consent
- Sex
- Race

- Ethnicity
- Baseline BMI (kg/m^2)
- Baseline SALT total score
- Initial alopecia areata subtype at disease onset, defined below
- Time since initial onset of alopecia areata, in years
- Alopecia areata subtype current episode
- Time since onset of alopecia areata current episode, in years
- Current Nail involvement
- Current Eyelash/eyebrow involvement
- Current other facial hair involvement

Time since initial onset of alopecia areata (years) and time since onset of alopecia areata current episode (years) will be computed as follows:

Lowest integer of [(Date of Screening visit – date of initial/current onset) / 365.25]

A by-patient listing of all demographics and other Baseline characteristics will be provided.

The patient's alopecia areata will be classified by the Investigator into one of three categories defined for this study:

1) Alopecia areata: patchy type hair loss,
2) Alopecia totalis or universalis: complete hair loss on the scalp with or without body hair loss,
3) Alopecia ophiasis: band-like hair loss limited to the periphery of the scalp along the back of the hair line in the occipital region and possibly extending over each ear in temporal regions.

The alopecia totalis and alopecia universalis category will be separated into each individual subtype for summaries.

9 SURGICAL AND MEDICAL HISTORY

Surgical and medical history will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA), version 22.0.

Surgical and medical history will be summarized for each dosing regimen by system organ class (SOC) and preferred term (PT) based on the Safety population. A patient who experienced the same surgical and medical history event multiple times within the same SOC will be counted only once for that SOC. Similarly, a patient who experienced multiple surgical and medical history events within the same PT will be counted only once for that PT. Surgical and medical history events will be sorted alphabetically by SOC and within each SOC, the PT will be presented by decreasing order.

A listing of all surgical and medical history events will be provided. All surgical and medical history for each patient in the Safety population will be included in a data listing.

10 PRIOR AND CONCOMITANT MEDICATIONS

Medications will be coded according to the World Health Organization Drug Dictionary (WHO-DD), March 2019 B3.

Prior medications are defined as any medication started and discontinued prior to the first dose of study drug. Concomitant medications are defined as all medications taken after the first dose of study drug, including dose who started prior to the first dose of study drug and continued past that date. See Appendix 3 for handling of completely or partially missing dates for prior and concomitant medications.

Frequency and percentage of prior and concomitant medications will be tabulated by Anatomical Therapeutic Chemical (ATC) term level 2 and preferred drug name by dosing regimen based on the Safety analysis population. A patient who took the more than one medication within the same medication ATC level 2 will be counted only once for that ATC level 2. Similarly, a patient who took more than one medication within the same preferred drug name will be counted only once for that preferred drug name.

A listing of all prior and concomitant medications will be provided.

11 STUDY TREATMENT EXPOSURE AND TREATMENT COMPLIANCE

A summary of exposure to study drug (days) will be presented by dosing regimen based on the Safety analysis population. Exposure to study drug, in days, will be computed as follows:

[(Date of last dose of study drug – Date of first dose of study drug) + 1]

Compliance with study drug (%) will be calculated as follow:

$$\frac{\text{Number of tablets taken}}{\text{Total number of tablets planned to be taken}} \times 100\%$$

where the number of tablets taken is defined as the total number of tablets dispensed minus the total number of tablets returned, and total number of tablets planned to be taken is defined as the exposure to study drug multiplied by the number of planned tablets per dose (i.e., 2).

Descriptive statistics for the compliance to study drug will be presented by dosing regimen based on the Safety population. Frequency distribution will also be presented for the following categories: < 80%, 80% - 120%, and > 120%.

Exposure and compliance will be displayed in a listing of study treatment administration.

12 EFFICACY ANALYSIS

12.1 Primary Efficacy Endpoint Analysis

The primary efficacy endpoint is the relative change from baseline in SALT score at Week 24. The SALT is a measure of hair absence that quantifies the amount of scalp surface without hair in a pre-specified quadrant of the scalp (right side [RRS], top [TRS], left side [LRS], and back [BRS]), that is further summed after applying a quadrant-specific multiplier indicative of scalp surface area contribution, to provide an overall score of total hair loss:

Total SALT Score = (LRS * 0.18) + (RRS * 0.18) + (TRS * 0.40) + (BRS * 0.24)

Refer to Section 6.2 for an important note about SALT absolute change from Baseline and relative change from Baseline endpoint definitions

Relative change in SALT score from Baseline to Week 24 will be summarized descriptively based on the mITT analysis population by dosing regimen. Difference of the means between the two

dosing regimens will also be provided along with a two-sided 90% Confidence Interval (CI). SALT data will be displayed in a by-subject data listing.

Line plots of means (+/- standard error of the mean [SEM]) SALT score over time by dosing regimen will be presented. Similar, line plots of means (+/- SEM) absolute change in SALT score and relative change from Baseline in SALT score over time by dosing regimen will also be provided.

Supportive Analysis

If applicable (refer to Section 4.2), the primary efficacy analysis will be repeated based on the PP analysis population.

Subgroup Analyses

Subgroup analyses by Baseline alopecia areata subtype (refer to Section 8 for the definition of Baseline alopecia areata subtype) will be performed.

12.2 Secondary Efficacy Endpoint Analyses

12.2.1 Responder Analysis: Proportion of patients achieving at least a 90%, 75%, and 50% in relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24

For the proportion of patients achieving at least a 90%, 75%, and 50% relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24, frequency and proportion will be presented by dosing regimen based on the mITT analysis population. The difference in proportions along with the two-sided Wald 90% CI (using the binomial approximation with a Wald continuity correction) will also be provided at each visit.

Additionally, line plots of proportions of patients over time by dosing regimen will be presented for the proportion of subjects achieving ate least a 50% in relative change from baseline only.

The same supportive and subgroup analyses as for the primary efficacy endpoint will be performed for this secondary efficacy endpoint (refer to Section 12.1).

12.2.2 Absolute change in SALT score from Baseline to Weeks 4, 8, 12, 16, 20, and 24, and relative change in SALT score from Baseline to Weeks 4, 8, 12, 16, and 20

For the absolute change in SALT score from Baseline to Weeks 4, 8, 12, 16, 20, and 24 as well as the relative change in SALT score from Baseline to Weeks 4, 8, 12, 16, and 20, a similar analysis approach as outlined for the primary efficacy endpoint (refer to Section 12.1) will be used, including the supportive and subgroup analyses.

12.2.3 Change in satisfaction of hair coverage as reported by the patient

The patient satisfaction hair coverage questionnaire will be assessed by the patient. The patient might select one of the five numeric choices representing "very dissatisfied" (0) to "very satisfied" (4). For consistency with the satisfaction of hair coverage quality questionnaire (see Section 12.3), responses to the satisfaction of hair coverage questionnaire will be rated 1 ("very dissatisfied") to 5 ("very satisfied") in the summaries and by-patient data listing. Missing data will not be imputed.

Responses to patient satisfaction question will also be summarized based on the mITT analysis population by category, visit, and dosing regimen using count and percentage.

The patient satisfaction hair coverage will be further categorized as 'satisfied' (i.e., including responses of 'somewhat satisfied', 'mostly satisfied', and 'very satisfied') or 'dissatisfied' (i.e., including responses of 'dissatisfied' and 'very dissatisfied'). A shift table will be presented for change in satisfaction of hair coverage (satisfied vs. dissatisfied) as reported by the patient based on the mITT analysis population for each scheduled visit and each dosing regimen.

No supportive and subgroup analyses will be performed.

Patient satisfaction of hair coverage data will be displayed in a by-subject data listing.

12.3 Exploratory Efficacy Endpoint Analyses

12.3.1 Change in patient's eyebrows as measured by the patient's Visual Analog Scale (VAS)

The VAS is a distinct 100-millimeter line anchored on the left end at full degree of impairment (no eyebrow) and on the right end at no degree on impairment (full eyebrow). Indication of the degree of impairment perceived at the time of assessment is captured by marking the appropriate position on the line between the anchor points. The measured distance of the mark from the left anchor will be recorded in millimeters. To assess the degree of impairment, the VAS analysis value will be computed by subtracting the VAS recorded value from 100. Missing data will not be imputed.

The VAS for each eyebrow will be summarized based on the mITT analysis population by visit and dosing regimen using descriptive statistics. The change and percent change from Baseline in VAS will also be summarized similarly for each eyebrow. Difference of the means in change and percent change from Baseline between the two dosing regimens will be provided along with a two-sided 90% CI at each visit for each eyebrow.

No supportive and subgroup analyses will be performed for this endpoint.

12.3.2 Change in satisfaction of hair coverage quality as reported by patient

The patient satisfaction hair coverage quality questionnaire will be assessed by the patient. For each of the 7 questions, the patient might select one of the five numeric choices representing "very dissatisfied" (1) to "very satisfied" (5). Missing data will not be imputed.

A similar analysis approach as outlined for the change in satisfaction of hair coverage secondary efficacy endpoint (refer to Section 12.2.3) will be used for the change in satisfaction of hair coverage quality total score. No supportive and subgroup analyses will be performed for this endpoint.

12.4 Other Efficacy Endpoint Analyses

12.4.1 Responder Analysis: Proportion of patients achieving at least 80% in relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24

The proportion of patients achieving at least 80% in relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24, frequency and proportion will be summarized and analyzed similarly to the proportion of patients achieving at least a 90%, 75%, and 50% relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24 (refer to Section 12.2.1).

12.4.2 Proportion of Subjects with a SALT Score ≤ 10 and ≤ 20 at Weeks 12 and 24

The number and percentage of subjects with a SALT score ≤ 10 and ≤ 20 at Weeks 12 and 24 will be summarized based on the mITT analysis population by visit and dosing regimen. The difference in percentages along with the two-sided Wald 90% CI will also be provided at each visit.

No supportive and subgroup analyses will be performed for this endpoint.

12.4.3 Global Impression Scales

The global impression scales employ a Likert scale measuring either disease severity or improvement after treatment. In this study, the global impression scales of severity and improvement will be performed by both the clinician and patient. The global impression scale of severity should consider the condition of the patient at the time of the assessment while the global impression scale of improvement should consider the condition of the patient at the time of the assessment compared to Baseline.

Clinical Global Impression of Severity (CGI-S)

The CGI-S will be assessed by the Investigator and will consider the severity of the patient's alopecia areata at the time of assessment. The Investigator may select one of the five numeric choices representing "Extremely severe" to "Not at all severe". Missing data will not be imputed.

Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. No statistical inferences will be performed for this endpoint.

No supportive analyses will be performed for this endpoint. Subgroup analyses by Baseline alopecia areata subtype will be provided.

Clinical Global Impression of Improvement (CGI-I)

The CGI-I will be assessed by the Investigator and will consider the Investigator's perceived change of the patient's alopecia areata at the time of assessment compared to Baseline. The Investigator may select one of the seven numeric choices representing "Very much worse" to "Very much improved". Missing data will not be imputed.

Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. The distribution of each treatment group across the different CGI-I categories will be compared using a Chi-square test.

Subjects will be further categorized at each visit as improved/not-improved in view of their response to the CGI-I. Improved subjects will be those who answered very much/much improved while not-improved subjects will be those who answered much worse or very much worse. Subjects with a missing value in CGI-I at a specific visit will be excluded from the analysis for that visit. Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. The distribution of each treatment group across the different CGI-I categories will be compared using a Chi-square test.

No supportive analyses will be performed for these endpoints. Subgroup analyses by Baseline alopecia areata subtype will be provided.

Patient Global Impression of Severity (PGI-S)

The PGI-S will be assessed by the patient and will consider the severity of his/her alopecia areata at the time of assessment. The patient may select one of the five numeric choices representing "Extremely severe" to "Not at all severe". Missing data will not be imputed.

Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. No statistical inferences will be performed for this endpoint.

No supportive analyses will be performed for this endpoint. Subgroup analyses by Baseline alopecia areata subtype will be provided.

Patient Global Impression of Improvement (PGI-I)

The PGI-I will be assessed by the patient and will consider the his/her perceived change of the patient's alopecia areata at the time of assessment compared to Baseline. The patient may select one of the seven numeric choices representing "Very much worse" to "Very much improved". Missing data will not be imputed.

Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. The distribution of each treatment group across the different PGI-I categories will be compared using a Chi-square test.

Subjects will be further categorized at each visit as improved/not-improved in view of their response to the PGI-I. Improved subjects will be those who answered very much/much improve while not-improved subjects will be those who answered much worse or very much worse. Subjects with a missing value in PGI-I at a specific visit will be excluded from the analysis for that visit. Frequency and percentages will be presented by category and visit based on the mITT analysis population for each dosing regimen. The distribution of each treatment group across the different PGI-I categories will be compared using a Chi-square test.

No supportive analyses will be performed for these endpoints. Subgroup analyses by Baseline alopecia areata subtype will be provided.

12.5 Summary of Efficacy Endpoint Analyses

Efficacy Endpoint	Collection Time	Method
Primary		
Relative change from Baseline in SALT score to Week 24	Baseline and Week 24	Descriptive statistics by visit and dosing regimen with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • *Supportive analysis*: using LOCF imputation based on PP analysis population, if applicable • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline
Secondary		
Responder (90%, 75% and 50%) in relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24	Baseline and Weeks 4, 8, 12, 16, 20, and 24	Count and proportion of subjects by visit and dosing regimen for each responder definition separately with difference in proportions and two-sided Wald 90% CI for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • *Supportive analysis*: using LOCF imputation based on PP analysis population, if applicable • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline

Efficacy Endpoint	Collection Time	Method
Absolute change from Baseline in SALT score to Weeks 4, 8, 12, 16, 20, and 24	Baseline and Week 4, 8, 12, 16, 20, and 24	Descriptive statistics by visit and dosing regimen with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • *Supportive analysis*: using LOCF imputation based on PP analysis population, if applicable • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline
Relative change from Baseline in SALT score to Weeks 4, 8, 12, 16, and 20	Baseline and Week 4, 8, 12, 16, and 20	Descriptive statistics by visit and dosing regimen with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • *Supportive analysis*: using LOCF imputation based on PP analysis population, if applicable • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline
Change from Baseline in satisfaction of hair coverage to Week 24	Baseline and Week 24	Descriptive statistics by visit and dosing regimen with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: with no imputation based on mITT analysis population • *Additional analysis*: shift from baseline (satisfied vs. dissatisfied) to each post-baseline visit with no imputation based on mITT analysis population • No supportive and subgroup analyses

Efficacy Endpoint	Collection Time	Method
Exploratory		
Change from Baseline in VAS for Eyebrows to Week 24	Baseline and Week 24	Descriptive statistics by visit and dosing regimen for each eyebrow separately with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: with no imputation based on mITT analysis population • No supportive and subgroup analyses
Change from Baseline in satisfaction of hair coverage quality to Week 24	Baseline and Week 24	Descriptive statistics by visit and dosing regimen with difference in means and two-sided 90% CI (t-distribution) for each post-baseline visit • *Main analysis*: with no imputation based on mITT analysis population • No supportive and subgroup analyses
Other		
Responder (80%) in relative change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24	Baseline and Weeks 4, 8, 12, 16, 20, and 24	Count and proportion of subjects by visit and dosing regimen for each responder definition separately with difference in proportions and two-sided Wald 90% CI for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • *Supportive analysis*: using LOCF imputation based on PP analysis population, if applicable • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline

Efficacy Endpoint	Collection Time	Method
Proportion of subjects with a SALT score of ≤ 10 and ≤ 20, at Weeks 12, and 24	Week 12, and 24	Count and proportion of subjects by visit and dosing regimen for each definition separately with difference in proportions and two-sided Wald 90% CI for each post-baseline visit • *Main analysis*: using LOCF imputation based on mITT analysis population • No supportive and subgroup analyses
Proportion of subjects in each CGI-S category at Baseline and Weeks 8, 12, and 24	Baseline and Weeks 8, 12, and 24	Count and proportion of subjects by category, visit, and dosing regimen • *Main analysis*: with no imputation based on mITT analysis population • No supportive analyses • *Subgroup analyses*: based on mITT analysis population within each subtype of alopecia areata at Baseline
Proportion of subjects in each CGI-I category at Weeks 8, 12, and 24	Weeks 8, 12, and 24	Count and proportion of subjects by category, visit, and dosing regimen • *Main analysis*: with no imputation based on mITT analysis population; distribution of each treatment group across the different categories will be compared using a Chi-square test • *Additional analysis*: Improved vs not improved at each post-baseline visit based on mITT analysis population; subjects with a missing CGI-I at a specific visit will be classified as not improved for that visit and distribution of each treatment group across the different categories will be compared using a Chi-square test at each visit. • No supportive analyses • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline

Efficacy Endpoint	Collection Time	Method
Proportion of subjects in each PGI-S category at Baseline and Weeks 8, 12, and 24	Baseline and Weeks 8, 12, and 24	Count and proportion of subjects by category, visit, and dosing regimen • *Main analysis*: with no imputation based on mITT analysis population • No supportive analyses • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline
Proportion of subjects in each PGI-I category at Weeks 8, 12, and 24	Weeks 8, 12, and 24	Count and proportion of subjects by category, visit, and dosing regimen • *Main analysis*: with no imputation based on mITT analysis population; distribution of each treatment group across the different categories will be compared using a Chi-square test • *Additional analysis*: Improved vs not improved at each post-baseline visit based on mITT analysis population; subjects with a missing CGI-I at a specific visit will be classified as not improved for that visit and distribution of each treatment group across the different categories will be compared using a Chi-square test at each visit. • No supportive analyses • *Subgroup analyses*: using LOCF imputation based on mITT analysis population within each subtype of alopecia areata at Baseline

13 SAFETY/TOLERABILITY ANALYSIS

All safety/tolerability analyses will be conducted based on the Safety analysis population by dosing regimen. No statistical inferences will be performed on any safety endpoint. All safety endpoints will be listed in by-patient data listings.

13.1 Adverse Events

AEs will be coded according to the MedDRA, version 22.0.

An AE reported after informed consent, but before the first dose of study drug (i.e., Day 1), will be considered a pre-treatment adverse event.

TEAEs are defined as any AEs with onset date/time on or after the first dose of study drug. See Appendix 3 for handling of completely or partially missing dates for AEs. In the case where it is not possible to define an AE as treatment emergent or not, the AE will be classified as treatment emergent.

An overall summary table of AEs will be provided. The frequency and percentage of patients who experienced at least one AE, TEAE, TEAE by greatest relationship with study drug, TEAE by highest severity/intensity, serious TEAE, treatment-related serious TEAE, TEAE leading to study drug discontinuation, TEAE leading to study drug dose interruption, TEAE leading to study discontinuation, and TEAE leading to death will be presented.

Frequency and percentage of patients who experienced TEAE will be summarized by SOC and PT. A patient experiencing multiple TEAEs within the same SOC will be counted only once for that SOC. Similarly, a patient experiencing multiple TEAEs within the same PT will be counted only once for that PT. TEAEs will be sorted alphabetically by SOC and PT will be presented by decreasing order of total frequency within each SOC. Serious TEAEs and treatment-related serious TEAEs will be summarized similarly.

Frequency and percentage of patients who experienced TEAE will be further broken down by greatest relationship to study drug. A treatment-related AE is defined as any TEAE that is assessed by the Investigator as definitely, probably or possibly related to study drug. A not related TEAE is defined as any TEAE that is assessed by the Investigator as unlikely related or not related to the study drug. TEAE with an unknown/missing relationship to study drug will be considered as treatment related. A patient experiencing multiple TEAEs within the same SOC will be counted only once for that SOC under the greatest relationship to study drug. Similarly, a patient

experiencing multiple TEAEs within the same PT will be counted only once for that PT under the greatest relationship to study drug.

Frequency and percentage of patients who experienced TEAE will be further broken down by highest severity (mild, moderate, and severe). TEAE with severity of life-threatening and fatal will be reported under the severe intensity category while TEAE with an unknown/missing severity will be considered as severe. A patient experiencing multiple TEAEs within the same SOC will be counted only once for that SOC under the highest severity. Similarly, a patient experiencing multiple TEAEs within the same PT will be counted only once for that PT under the highest severity.

Listings of all AEs, all AEs leading to death, all serious AEs, all TEAEs leading to study drug discontinuation and all TEAEs leading to study discontinuation will be provided.

13.2 Clinical Laboratory

Descriptive statistics will be presented by dosing regimen at Baseline and each post-Baseline visit for data related to chemistry, hematology, and lipids tests. Change from Baseline values will also be presented at each post-Baseline visit.

Separate listings will be provided for abnormal (low or high) chemistry (including lipids) and hematology laboratory results. Clinical laboratory results that fall outside the central laboratory reference range will be interpreted by the Investigator as Abnormal, not clinically significant (NCS) or Abnormal, clinically significant (CS). Abnormal, NCS and Abnormal, CS laboratory values will be flagged in the by-subject data listings.

Additionally, treatment-emergent potentially clinically significant (PCS) laboratory values will be identified. Potentially clinically significant values are defined as those that meet Grade 3 or Grade 4 toxicity criteria from the common terminology criteria for AEs (CTCAE) criteria. Treatment-emergent PCS laboratory values are those in which the Baseline value is not PCS and the post-Baseline value is PCS. Frequency and percentage of patients with treatment-emergent PCS laboratory values at any time on treatment will be summarized by dosing regimen for each clinical laboratory variable Frequency and percentage of patients with treatment-emergent PCS laboratory values will also be summarized by dosing regimen and post-Baseline visit for each clinical laboratory variable.

Line plots of means (+/- SEM) in laboratory value over time by dosing regimen will be presented for each hematology parameter of interest (i.e., hemoglobin, absolute neutrophils count, platelets, and reticulocytes).

Separate listings of all data for chemistry, hematology, lipids, serum pregnancy, serology, and other laboratory tests will also be provided. Treatment-emergent PCS laboratory values that result in dose interruption will be identified in these listings.

13.3 Vital Signs

Descriptive statistics will be presented by dosing regimen at Baseline and each post-Baseline visit for data related to vital signs (systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, oral temperature, and weight). Change from Baseline values will also be presented at each post-Baseline visit.

A by-patient listing of all vital sign assessments will be provided.

13.4 Physical Examination

Clinically significant deteriorations in physical examination findings will be reported and summarized as adverse events.

A listing of all physical examination assessments will be provided.

13.5 Electrocardiogram

Descriptive statistics will be presented by dosing regimen at Baseline and each post-Baseline visit for data related to ECG parameters (PR, QT, QTcF, QRS, and RR). Change from Baseline values to each post-Baseline visit will be presented.

Additionally, count and percentage of subjects with a QTcF value < 450 msec at Baseline but > 450 msec, > 480 msec, > 500 msec at any time on treatment will be provided. Count and percentage of subjects with a QTcF value < 450 msec at Baseline but a value > 450 msec, > 480 msec, > 500 msec will also be provided for each post-baseline visit. QTcF increase from baseline > 30 msec and > 60 msec among subjects with a QTcF value < 450 msec at Baseline will be summarized similarly.

A by-patient listing of ECG assessments will be provided, including the Investigator's overall ECG interpretation (normal, abnormal NCS, and abnormal CS).

14 APPENDICES

Appendix 1

Table 1 provides a description of the procedures planned at each visit.

Table 1: Schedule of Events

Event	Screening	Randomization[1]	Treatment Period					Safety Follow-Up
	Day -28 to Day -1 (Visit 1)	Day 1[2] (Visit 2)	Week 2, 6 (Visit 3, 5)	Week 4, 8 (Visit 4, 6)	Week 12 (Visit 7)	Week 16, 20 (Visit 8, 9)	Week 24[3]/ET (Visit 10)	Week 28[4] (Visit 11)
Informed consent	X							
Eligibility assessment	X	X						
Demographics	X							
Medical and surgical history	X	X						
Randomization		X						
Physical examination	X	X					X	X
Brief physical examination				X	X	X		
Height	X							
Weight	X	X		X	X	X	X	X
Pregnancy test[5]	X	X	X	X	X	X	X	X
Tuberculosis test[6]	X							
Clinical laboratory testing[7 8]	X[9]	X	X	X	X	X	X	X
Lipid assessment[10]		X			X		X	X
HBV and HCV test	X							
12-lead electrocardiogram	X	X			X		X	X
Vital signs	X	X		X	X	X	X	X
Severity of Alopecia Tool (SALT) assessment[11]	X	X		X	X	X	X	
Photographs[12]	X	X			X		X	
Patient Satisfaction Questions	X	X		X[13]	X		X	
Visual Analog Scale (VAS) for Eyebrows		X			X		X	
Clinical Global Impression of Severity	X	X		X[13]	X		X	
Clinical Global Impression of Improvement				X[13]	X		X	
Patient Global Impression of Severity	X	X		X[13]	X		X	
Patient Global Impression of Improvement				X[13]	X		X	
Study Product Administration at study site		X	X	X	X	X		
Dispense study drug		X		X	X	X		
Study drug accountability				X	X	X	X	
Adverse events[14]	X	X	X	X	X	X	X	X
Concomitant medications[14]	X	X	X	X	X	X	X	X

ET=Early termination; HBV= hepatitis B virus; HCV = hepatitis C virus; PPD = purified protein derivative.

[1] Randomization/Day 1 may occur any time after Screening laboratory results are available and reviewed by the Investigator.

[2] All subsequent visits and week increments should be based on the date of Visit 2. All visit windows are ±3 days for subsequent visits.

[3] Also serves as the Early Termination Visit for patient withdrawal in this period.

[4] The Safety Follow-Up Visit is intended for those patients who do not roll over into an open-label extension and for patients who have been discontinued from the study and completed the Early Termination Visit (Week 24).

[5] For females of childbearing potential, a serum pregnancy test will be performed at all visits aside from the randomization visit where a urine pregnancy test will be performed.

[6] If PPD (skin test) is performed, subject will need to return to the clinic 24-48 hours after placement for PPD reading.

[7] Includes hematology and serum chemistry.

[8] When possible, collect pre-dose, except on Visit 11.

[9] Will include thyroid stimulating hormone and hemoglobin A1c at Screening only.

[10] Includes total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides.

[11] Should be performed by the same rater, when possible, for the patient for the duration of the study.

[12] For participants who authorize photographs to be taken of their scalp involvement and/or eye and nail involvement.

[13] Will be conducted at Visit 6 (Week 8) only.

[14] Collection is ongoing.

Appendix 2

Output Conventions

TLF will be generated using SAS® and will be displayed on letter size paper with landscape orientation, 1-inch margins, and 9-point Courier New font.

All TLFs will include a header section comprised of the Sponsor's name, the protocol number, the delivery description, the data cut-off date (if applicable), the TLF number, the TLF title, the analysis population, and the page number (Page X of Y). The footer section will include the TLF footnotes, the CRO's name, the date and time of the execution of the program, and the name of the program.

Summary tables and data listings will be summarized by dosing regimen and overall, as appropriate. All data collected per-protocol and all derived variables will be listed.

Mean and median will be displayed to one more decimal place than the original value; SD and CI will be displayed to two more decimal places than the original value; minimum and maximum will keep the same number of decimal places as the original value. If derived parameters are to be summarized, the number of decimals of the derived values is to be chosen on a case-by-case basis, but the rule above applies.

For categorical summary tables, percentages will be reported to one decimal place. Percentages between 0 and 0.1 (both exclusive) will be displayed as "<0.1". Percentages between 99.9 and 100.0 (both exclusive) will be displayed as ">99.9". For each dosing regimen, the denominator for each percentage will be the number of patients within the population, unless otherwise specified.

Listings will be ordered by dose regimen, patient number, parameter (where applicable), date, and visit (where applicable). Imputed dates and imputed missing data will not be presented in the listings.

All statistical deliverables will be produced, validated, and reviewed for accuracy/consistency in accordance with [redacted] standard operating procedures.

Dates & Times Format

Date and time (if available) will be presented in the format yyyy-mm-dd/hh:mm.

Presentation of Treatment Arms

When applicable, study treatments will be represented as follows in the different outputs:

Study Treatment Full Names	Study Treatment Output Names
12 mg BID CTP-543	12 mg BID CTP-543
24 mg QD CTP-543	24 mg QD CTP-543

Appendix 3

Algorithm for Imputation of Start/End Date of Adverse Events and Prior/Concomitant Medications

Event Start Date Imputation

- Imputation of event end date should be done before imputation of event start date.
- Completely missing: Impute to the date of the first dose of study treatment.
- Missing day and month: Impute to January 1st, unless year is the same as year of first dose of study treatment. If so, impute to the date of the first dose of study treatment.
- Missing day: Impute to the 1st of the month, unless month and year are the same as month and year of first dose study treatment. If so, impute to the date of the first dose of study treatment.
- If imputed event start date is after event end date (imputed or not), set the event start date to the imputed event end date.

Event End Date Imputation

- Completely Missing: Impute to the date of the last dose of study treatment.
- Missing day and month: Impute to December 31st, unless year is the same as the date of the last dose of study treatment. If so, impute to the date of the last dose of study treatment.
- Missing day: Impute to the last day of the month, unless year and month are the same as year and month of the date of the last dose of study treatment. If so, impute to the date of the last dose of study treatment.